2,218,148

UNITED STATES PATENT OFFICE

2,218,148

MANUFACTURE OF BENZENE HEXA-CHLORIDE

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4 Claims. (Cl. 260—648)

This invention relates to the manufacture of benzene hexachloride by the chlorination of benzene. More particularly, it is concerned with an improved process for the manufacture of benzene hexachloride wherein the chlorination is interrupted before the total quantity of benzene present has been converted into the hexachloride, the solid product removed by filtration, and the filtrate, after the addition of further amounts of benzene, subjected to further chlorination.

In the preparation of benzene hexachloride, it has already been proposed to chlorinate benzene in the presence of a large volume of dilute alkali. However, this process is inefficient and results in only relatively poor yields of the hexachloride.

A process wherein the benzene is treated with chlorine, preferably in the presence of light, the liquid becoming more viscous as chlorination proceeds until finally an almost solid mass is obtained, is also known to chemists. However, this method presents mechanical difficulties in the subsequent purification steps in that the incompletely chlorinated products are not easily removed.

I have now found that these disadvantages in the preparation of benzene hexachloride by the direct chlorination of benzene in the presence of actinic radiation may be avoided by stopping the reaction at a point wherein the liquid contains an amount of solid product which is not too great to be easily separated by filtration. Preferably, temperatures below about 20° C. are employed. When the reaction product is partially converted to the solid benzene hexachloride, the solid product is removed by filtration and the filtrate, after the addition of further quantities of benzene, again subjected to the action of chlorine in the presence of actinic light. The chlorination is preferably carried out in the absence of those metals which tend to promote the formation of substituted benzenes to any substantial extent.

By this means a continuous process for the manufacture of benzene hexachloride results, which process does not necessitate troublesome mechanical treatment or the filtration of extremely thick slurries in order to obtain the desired solid hexachloride. By stopping the chlorination when the reaction mixture is not too thick to permit ready filtration, filtering to remove the solid product, thereafter diluting the filtrate by the addition of further amounts of benzene and subjecting to further chlorination, yields are obtained which are high or as high as

can be obtained by other known methods. By reworking the filtrate after the removal of the solid product the formation of mono- and disubstituted chloro benzenes is greatly reduced.

The amount of solid product which may be allowed to accumulate in the reaction liquid before being removed by filtration is not critical. I have found in practice that it is desirable to interrupt the chlorination and filter off the solid product when approximately half of the theoretical quantity of chlorine has been absorbed. Similarly, the amount of benzene which should be added to the filtrate before the second chlorination is begun is again not critical. However, it is convenient to add such a quantity of benzene that the reaction mixture is made up to its original bulk.

After the process has been continued for some time, quantities of benzene substitution products will accumulate in the reaction mixture, even though, as has been previously stated, the described process tends to diminish the formation of such products. It is therefore necessary at infrequent intervals to reject the filtrate after the solid product has been filtered off and to recommence the process by chlorinating a fresh batch of benzene.

The following example illustrates one method of carrying out my invention. In this example all parts specified are by weight.

Example

Chlorine gas was gradually passed into 660 parts of benzene contained in a lead-lined reaction vessel until 890 parts of the gas had been absorbed. The mixture was stirred continuously and the temperature maintained at 15 to 20° C.

The supply of chlorine was then interrupted and the precipitated solid filtered off and dried. In weight, it was found to be equivalent to 900 parts. The mother liquid was then mixed with 330 parts of benzene and the mixture again treated with 890 parts of chlorine in the manner described.

After filtering the reaction mixture resulting from the second chlorination, the filtrate was again mixed with a smaller quantity of benzene and again chlorinated in a similar manner. In this way, a continuous process for the preparation of benzene hexachloride resulted.

Since various changes and modifications may be made in my process as described, I do not desire to be limited to the exact temperatures nor to exact amounts and procedural details. The

scope of my invention is to be construed in accordance with the appended claims.

I claim:

1. A process for preparing solid benzene hexachloride which comprises chlorinating liquid benzene in a non-aqueous system with gaseous chlorine in the presence of actinic light and in the essential absence of substitution chlorination metal catalysts until a portion of the benzene present is converted into solid benzene hexachloride in amount easily separable by filtration, filtering off the solid product, adding fresh benzene to the filtrate and subjecting said enriched filtrate to further chlorination.

2. A process for preparing solid benzene hexachloride which comprises chlorinating liquid benzene in a non-aqueous system with gaseous chlorine in the presence of actinic light at a low temperature within the range wherein benzene is liquid at ordinary pressure and in the essential absence of substitution chlorination metal catalysts until a portion of the benzene present is converted into solid benzene hexachloride in amount easily separable by filtration, filtering off the solid product, adding fresh benzene to the filtrate and subjecting said enriched filtrate to further chlorination.

3. A process for preparing solid benzene hexachloride which comprises chlorinating liquid benzene in a non-aqueous system with gaseous chlorine in the presence of actinic light at a temperature below 20° C. and in the essential absence of substitution chlorination metal catalysts until a portion of the benzene present is converted into solid benzene hexachloride in amount easily separable by filtration, filtering off the solid product, adding fresh benzene to the filtrate and subjecting said enriched filtrate to further chlorination.

4. A process for preparing benzene hexachloride which comprises chlorinating liquid benzene in a non-aqueous system with gaseous chlorine at a temperature below 20° C. in the presence of actinic light and in the essential absence of substitution chlorination metal catalysts until approximately one-half the theoretical quantity of chlorine for hexachloride production has been absorbed, filtering off the solid product, adding fresh benzene to the filtrate and subjecting said enriched filtrate to further chlorination.

THOMAS HARDIE.

E. ULMANN

LINDANE

Monograph of an Insecticide

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VERLAG K. SCHILLINGER · FREIBURG IM BREISGAU

1972

A. INTRODUCTION

by D. DEMOZAY and G. MARECHAL (Lyon)

Definition — History — General Facts

By virtue of its chemical structure and biological properties, lindane holds a unique place among chlorinated organic insecticides. It should not be confused with benzenehexachloride (BHC), a mixture of various isomers and byproducts, which was discovered by FARADAY in 1825. Its insecticidal properties were first demonstrated by the American chemist BENDER in 1933, and later by the French chemist A. DUPIRE during an independent study in 1940. Besides Dupire, chemists and biologists of Imperial Chemical Industries Ltd. also recognized the insecticidal property of lindane. BHC is a mixture of various stereo isomers (alpha, beta, gamma, delta, epsilon etc.) and complex chlorinated structures, such as heptachlorocyclohexanes and octachlorohexanes.

Only the gamma isomer possesses insecticidal properties.

The pure gamma isomer (with a degree of purity of at least 99 %) has been named lindane after the Belgian chemist VAN DER LINDEN, who in 1912 first discovered its existence.

Because of the presence of the inactive isomers (α, β, δ, ϵ) technical BHC shows properties which differ widely from those of lindane.

Lindane has been defined in precise chemical terms. It is odourless, inexpensive to manufacture, very active against most types of insects and has proved to have virtually no drawbacks. Its low toxicity at the time of application, the quick disappearance of the residue from the plant, the fact that it only needs to be applied at low concentration — all of these facts, make lindane an insecticide which should hold the interests of potential users and specialists in hygiene for a considerable period of time to come. The task of such experts is to provide foodstuffs in ever increasing quantity and quality to meet the needs of an ever expanding world population which must be protected from epidemics and hunger without being exposed to the danger of environmental pollution.

The amount of literature on lindane which has been accumulating makes a complete review very difficult. Therefore, this book does not aim at an exhaustive review of all available papers, but rather at assisting potential users, toxicologists, entomologists, ecologists etc., who are concerned with the use of pesticides, in answering questions which may arise in connection with lindane.

Manufacture of Lindane

Lindane is extracted from technical BHC and the process can be simplified as follows:

1. BHC is synthesized by the direct action of chlorine on benzene in the presence of ultra violet light.
   It is desirable to produce tech. BHC with the highest possible gamma isomer content (15 %). By-products are avoided by careful control of the conditions (temperature and concentration).

2. Extraction of Lindane.
   Lindane is extracted from BHC by the use of selected solvents, the most common of which is methyl alcohol.
   In this way the gamma isomer with a purity of over 99 % is obtained.
   Treatment of the active ingredient with nitric acid virtually eliminates the remaining traces of odour.
   In this way a product is obtained, which as mentioned earlier, has very different biological properties from BHC and is practically odourless.

B. PHYSICAL AND CHEMICAL PROPERTIES
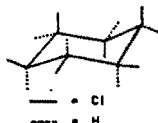
by D. DEMOZAY and G. MARECHAL (Lyon)

Physical and Chemical Data *

International common name:	Lindane (AFNOR — ISO)
	(BSI common name = GAMMA-BHC = lindane)
	Germany = Lindan
	USSR = lindane
Chemical name:	The gamma isomer of 1, 2, 3, 4, 5, 6
	Benzene hexachloride = Hexachlorocyclohexane
Molecular weight:	290,9

Structural formula:

— = Cl
--- = H

Melting point:	112,8°C

Vapour pressure:	SLADE (1945)	BALSON (1947)	SPENCER-CLIATH (1970)
	0,03 mmHg at 20°C	$9,4 \times 10^{-6}$ mmHg at 20°C	$3,26 \times 10^{-5}$ mmHg at 20°C
	0,14 mmHg at 40°C		$45,6 \times 10^{-5}$ mmHg at 40°C
	0,48 mmHg at 60°C		

Density:	1,85
Appearance:	a white crystalline solid
Smell:	faint to odourless
	(the characteristic musty odour of technical BHC is attributed to the presence of impurities, especially heptachlorocyclohexane)

Solubility

The solubility of lindane is summarized in the following table:

SLADE (1945); KAUER (1947); NEGHERBON (1959); BEZOBRAZOV (1958).

The solubility of lindane in water varies with temperature:

7,3 ppm at 25°C, 12 ppm at 35°C, 14 ppm at 45°C (RICHARDSON-MILLER cited by GUNTHER et al., 1968).

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* For detailed information on manufacture and physical-chemical properties see BEZOBRAZOV et al. (1958) METCALF (1965)

Table 1 Solubility

| SOLVENT	Solubility of the various isomers in 100 g solvent at 20 °C				
	α	β	Lindane	δ	ε
Ethyl acetate	12,7	6,9	35,7	58,5	
Acetone	13,9	10,3	43,5	71,1	33,2
Acetic acid	4,2	1	12,8	25,6	
Butyl alcohol	1,6	0,7	4,4	19,4	2,4
Ethyl alcohol	1,8	1,1	6,4	24,2	4,2
Benzene	9,9	1,9	28,9	41,1	
Chloroform	6,3	0,3	24	13,7	2
	17,3	12,1	36,7	49,4	
Dioxene	33,6	7,8	31,4	58,9	
Petrol ether 80 — 100°C	1	0,2	2,9	3,2	0,3 *
Ether	6,2	1,8	20,8	35,4	3
Diesel oil	1,5	0,3	4,1	9,2	
White oil	0,7	0,02	1,9	1,1	
Methanol	2,3	1,6	7,4	27,3	3,7
Carbon tetrachloride	1,8	0,3	6,7	3,6	0,5
Toluene	9	2,1	27,6	41,6	
Trichlorethylene	3,7	0,3	14,7	7,6	
Xylene	8,5	3,3	24,7	42,1	
Distilled water	10 ppm	5 ppm	10 ppm	10 ppm	

* fraction 60—80 °C
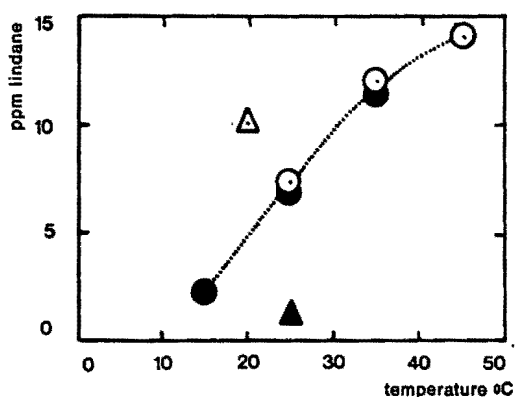
Figure 1 Solubility of lindane in water

○ according to GUNTHER et al. (1968)
● according to BIGGAR et al. (1966)
    for a particle size of 5.0 μ
▲ according to BIGGAR et al. (1966)
    for a particle size
    of 0.05 μ
△ according to SLADE (1945)

Stability

Lindane is stable to light, heat, air, carbon dioxide and strong acids.

It is unstable in the presence of alkali, producing trichlorobenzenes and hydrochloric acid. KAUER (1947); LaCLAIR (1948); BEZOBRAZOV (1958).

Lindane decomposes in the presence of certain powdered metals such as iron, aluminium and zinc. The presence of water appears to be necessary for this reaction, and the more easily a metal ionises the more readily the decomposition occurs.

(Because of this latter property fumigation containers of copper, porcelain, pyrex etc., are preferable).

Spatial Structure of Lindane and other BHC Isomers

Theoretically BHC can exist as 17 optical or stereo isomers. However spatial and energy system considerations show that only 9 of these isomers are possible.

ORLOFF (1954) has shown that of all the hypotheses on the structural form of BHC, the most probable is the trans form (chair form). The alpha isomer exists as two racemic forms (optical isomers).

The α, β, γ, δ, ϵ, ζ isomers are present in technical BHC in considerable quantities and result from the chlorination of benzene. The η and θ isomers arise from the chlorination of tetrachlorocyclohexene which can also give the ζ isomer.

MENNIER (1884); VAN DER LINDEN (1912); KAUER (1947); KOLKA et al. (1952 – 1954); RIEMSCHNEIDER (1953).
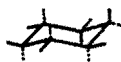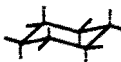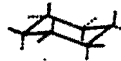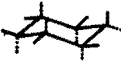

"chair" (trans)   "boat" (cis)

Comparison of the Physical Constants of Lindane and some of the other BHC Isomers

Table 2   BEZOBRAZOV (1958); EICHLER (1965); MELNIKOV (1971)

Isomer	% in techn. BHC	Melting point	Vapour pressure mmHg 20 °C	Polarity	Refraction index nD 20	Wave lnegth in angströms	Configuration Cl ···· H	Crystal
α	60-70	157,5-158,5	0,02	2,22:	1,60 -1,626	1258		monoclinic prisms
β	5-12	309	0,005	0	1,630	1346		cubic (octahedral)
γ	10-15	112,8	0,03	2,8: 3,6	1,60 -1,635	1322		monoclinic crystals
δ	6-10	138-139	0,02	2,2: (2,17: 2,32)	1,576-1,674	1181		crystals or fine platelets
ε	3- 4	218,8		0	1,00 -1,635	1396		monoclinic needles or
ζ		69 - 88						hexagonal
η		89,8- 90,5						monoclinic
θ		124 -125						crystals

The above mentioned values for vapour pressure are those published by SLADE (1945). In contrast BALSON (1947) has recorded substantially lower values e. g. 9.4×10^{-6} mmHg at 20°C for lindane. Recently SPENCER and CLIATH 1940 have reported 3.26×10^{-5} mmHg at 20°C. Using a saturation dynamic method and quantities normally required in gas chromatography. The authors have since established a value of 1.6×10^{-4} mmHg at 20°C.

Crystal structure depends on the type of solvant used e. g. needles with acetic acid and rhomboids with chloroform .

Lindane differentiates itself from these other isomers of BHC particularly in respect of its lower melting point, its higher vapour pressure (which explains is relative lack of persistance in comparison to technical BHC) and its more marked polarity, which explains its weaker affinity for fat.

Comparison of the Structure of Lindane with other Organo-Chlorine Insecticides

The most important chlorinated organic insecticides fall into two basic groups: those with two phenyl groups and those containing a cyclodiene. Examination of the chemical structure of the lindane molecule shows it to be markedly different. Because of this structural difference lindane has biological properties which often contrast strongly with the other chlorinated insecticides.
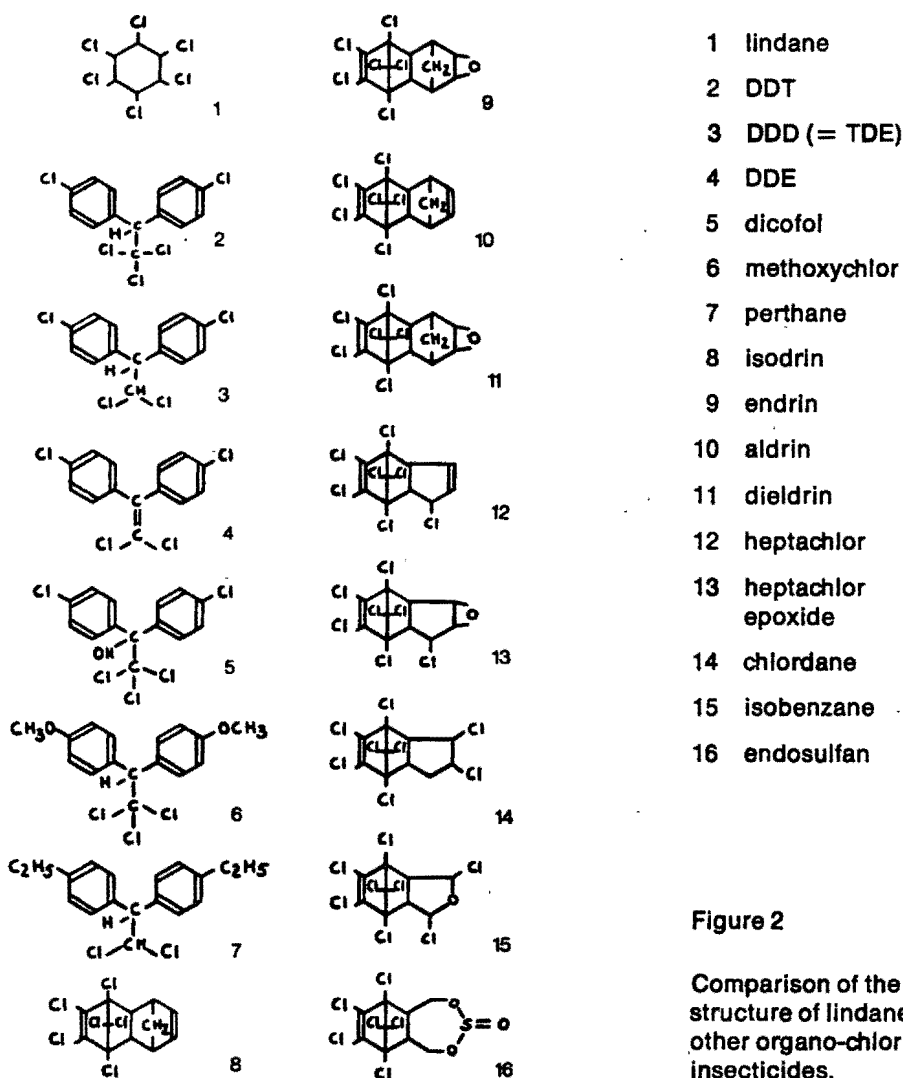

1 lindane
2 DDT
3 DDD (= TDE)
4 DDE
5 dicofol
6 methoxychlor
7 perthane
8 isodrin
9 endrin
10 aldrin
11 dieldrin
12 heptachlor
13 heptachlor epoxide
14 chlordane
15 isobenzane
16 endosulfan

Figure 2

Comparison of the structure of lindane with other organo-chlorine insecticides.

Comparison of the Physical Constants of Lindane with other Common Insecticides

Compared with the common insecticides and particularly those with chlorinated structures, lindane has a high vapour pressure. This quality together with its stability to heat explains its suitability for use in fumigation.

For ease of comparison the vapour pressures of some important compounds are listed graphically in Figure 3.

Table 3

Name	Melting point °C	Vapor pressure mmHg 20 °C	Water solubility ppm
Aldrin	104 — 105	4×10^{-6}	0,07 (21 °C)
Dieldrin	175 — 176	$1,8 \times 10^{-7}$	0,05 (21 °C)
DDT pp'	108,5	$1,9 \times 10^{-7}$	~ insoluble
Endrin	200 (decomposes)	2×10^{-7} (25 °C)	0,06 (25 °C)
Heptachlor	95 — 96	3×10^{-4} (25 °C)	~ insoluble
Isobenzane	120 — 122	3×10^{-6}	~ insoluble
Amidithion	46	8×10^{-6}	20 000
Azinphos ethyl	53	10^{-6}	~ insoluble
Monocrotophos	25 — 30	7×10^{-7}	soluble
Carbophenothion	liquid	3×10^{-7}	0,34
Dimethoate	50 — 52	$2,5 \times 10^{-2}$	25 000
Fenitrothion	liquid	5×10^{-5}	20
Malathion	2,8	10^{-4}	145
Parathion	liquid	$3,8 \times 10^{-5}$	20
Ronnel	35 — 37	8×10^{-4} (25 °C)	40 (25 °C)
Trichlorfon	78 — 80	8×10^{-6}	154 000
Carbaryl	142	$<5 \times 10^{-3}$ (25 °C)	~ 1 000
Arprocarb	86 — 91	10^{-2} (120°C)	~ 1 000
Minacide	87	10^{-1}	~ insoluble
LINDANE	112,8	$3,26 \times 10^{-5}$	10
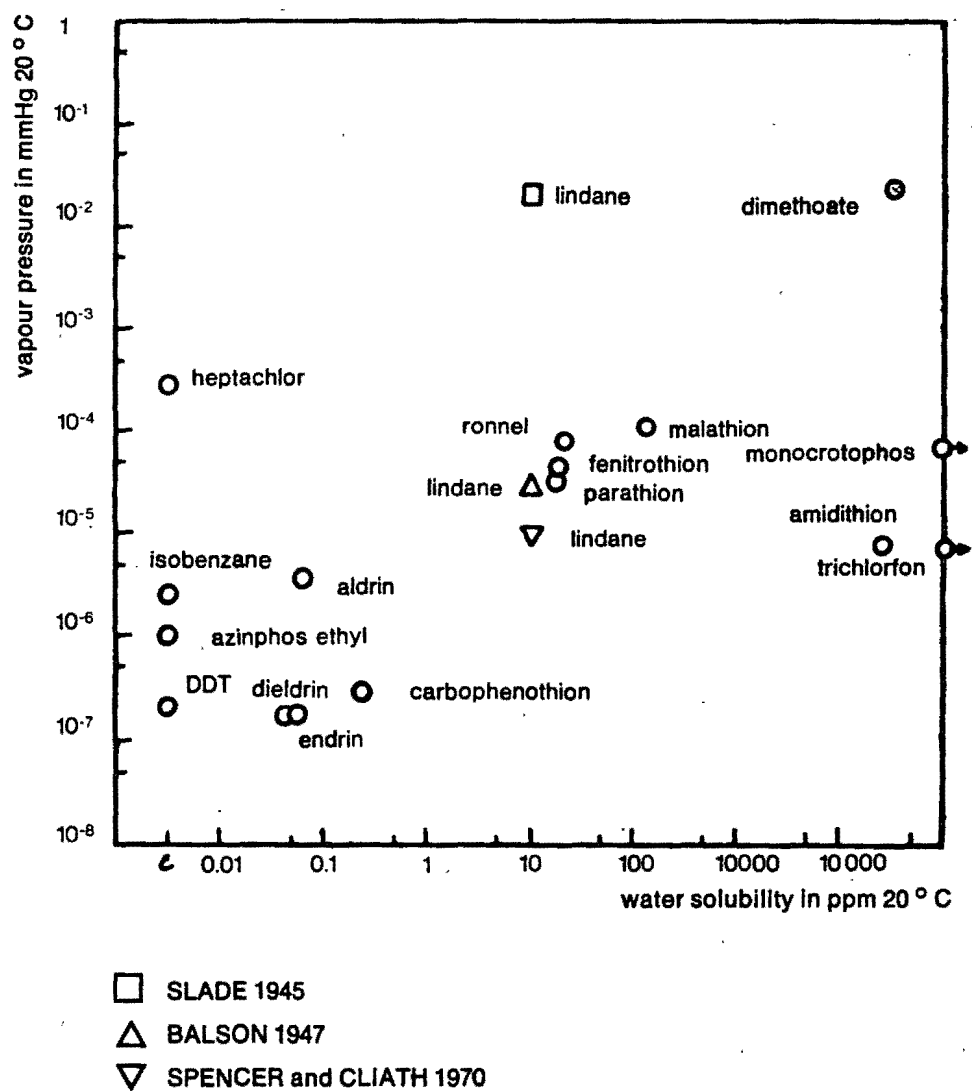
Figure 3   Vapour pressure and water solubility of various insecticides

It has been mentioned several times already that lindane cumulates in soil to a lesser extent than other chlorinated hydrocarbon insecticides. An important reason for this lies in the quantitatively different adsorption and desorption properties of the mineral and organic soil components.

SWANSON et al. (1954) found clear correlations between sorption and the content of clay minerals; for example, the adsorption of lindane in a silt loam is about 20 times as high as that in a clay sand.

The adsorption/desorption equilibria of lindane on living organic matter have been studied in model experiments with bakers' yeast. Lindane is at first taken up by yeast cells from an aqueous solution, but is then rapidly desorbed again by fresh water (VOERMAN and TAMMES, 1969). These findings explain the fact that lindane may be present in relative abundance in ground water without occurrence of a significant uptake by living organisms. Waters contaminated with various pesticides showed relatively high lindane residue levels, whereas the residue concentrations in the plants and fish living in these waters were toxicologically insignificant. By contrast, DDT was found in only a low concentration in the water, but in substantial concentrations in plants and fish (ABBOTT et al., 1965).

— Breakdown by Microorganisms

The relatively low stability of lindane in soil is due partly to its breakdown by microorganisms. As long ago as 1946, WALLACE showed with biotests that the efficacy of lindane in the control of *Heteronychus sanctae-helenae (Blanch.)* was limited to 4 to 6 months. LICHTENSTEIN et al. (1966), studying insecticides in waters, also found that lindane is subject to substantial microbial breakdown. These findings were confirmed by MacRAE et al. (1969). In these experiments lindane was broken down substantially more slowly in autoclaved, i. e., biologically dead soil than in non-sterile soil. The fact that a second dose of lindane added to non-sterilised soil samples at a later date was broken down even faster than the first dose led to the conclusion that lindane promotes the growth of soil microorganisms with specific lindane-degrading activity.

Green algae (*Chlorella* species) also break down lindane in water (MAIER-BODE, 1965). In waters heavily contaminated with faeces, urine and other organic impurities, lindane is destroyed by bacteria, whereas technical grade BHC is not (ALLAN, 1965).

Under anaerobic conditions lindane is usually metabolised more rapidly than other chlorinated hydrocarbon pesticides. This is evidently due to anaerobic organisms such as *Escherichia coli*. The previously mentioned rapid disappearance of lindane from flooded tropical soils is due to the same cause (MacRAE et al., 1967). These authors have isolated an anaerobic, gram-negative bacterial species which breaks down lindane exceptionally fast. For example, the lindane concentration dropped within 11 days from 3.7 to 0.03 ppm. In pure culture the drop within 27 hours was from 3.67 to 0.02 ppm (MacRAE et al., 1969).

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Little is known on the structure of the breakdown products. YULE et al. (1967) have found small quantities of γ-pentachlorocyclohexene. LICHTENSTEIN et al. (1971) found in addition 1,2,3,4-tetrachlorobenzene as well as other unidentified compounds. NEWLAND et al. (1969) have reported on the isomerisation of lindane to α- and δ-hexachlorocyclohexane, but this observation was not confirmed by other authors (YOSHIDA and CASTRO, 1970).

It may be stated in summary that, compared with other chlorinated hydrocarbon insecticides such as aldrin, dieldrin, heptachlor and DDT, lindane disappears from soil relatively rapidly. The main reasons for this are:

1. Low application rate, made possible by high insecticidal potency.
2. Rapid evaporation owing to a high vapour pressure and good entrainment by water vapour.
3. Rapid dilution in the soil by diffusion.
4. Low adsorption on dead organic matter and by plants.
5. Breakdown by microorganisms.

The breakdown processes in soil, particularly the metabolic processes, are relatively little known and require further investigation.

Lindane Residues in Water and Fish

As a result of their many and diverse uses, pesticides may get into water in a variety of ways. It is obvious, for example, that insecticides used for the control of mosquitoes in lake and river areas come directly into contact with water. However, the use of insecticides in agriculture and forestry may also result in an undesirable contamination of waters. Pesticides bound to soil particles may be desorbed by rain-water or may be carried together with the soil particles down gradients into streams, lakes or reservoirs. Waters may also be contaminated by liquid waste from pesticide manufacturing plants and by fallout from the atmosphere.

WEAVER et al. (1965) found dieldrin, endrin, DDT and its breakdown product DDE, as well as much smaller quantities of heptachlor and aldrin in all the major rivers in the USA, whereas BHC was detected at only one monitoring station.

In a qualitative and quantitative study of the waters of the Ohio river, the total concentration of the residues of all identified chlorinated hydrocarbon insecticides (aldrin, BHC, chlordane, DDD, DDT, dieldrin, endrin and methoxychlor) was less than 10 ppb (1 ppb = 0.001 ppm = 1 mcg/kg). There is no mention of lindane in this list (ROSEN and MIDDLETON, 1959). The authors consider the analysis method

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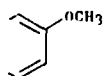:ther.

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myces lincolnensis*

Second column

var. *lincolnensis:* Mason *et al.,* and Herr, Bergy, *Antimicrobial Agents & Chemotherapy* 1962, 555 and 560; Bergy, Herr and Bergy *et al.,* U.S. pats. 3,086,912 and 3,155,580 (1963 and 1964, both to Upjohn Co.). Structure: Hoeksema *et al., J. Am. Chem. Soc.* 86, 4223 (1964).
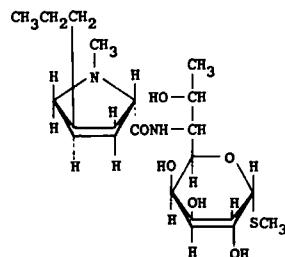
Free base, pK$_a'$ 7.6. No ultraviolet absorption max (220–400 mμ). More stable in salt form. Soluble in methanol, ethanol, butanol, isopropanol, ethyl acetate, *n*-butyl acetate, amyl acetate, acetone, methyl ethyl ketone, isopropyl *n*-butyl ketone, methylene chloride, chloroform, ethylene dichloride. Somewhat sol in water. *See:* Bergy *et al., loc. cit.*

Hydrochloride, C$_{18}$H$_{34}$N$_2$O$_6$S.HCl.½H$_2$O, *Frademicina, Lincocin, Mycivin.* Formerly obtained as needle-like crystals of low sp gr from aq soln by rapid addition of acetone at low temps; now obtained as crystals of higher sp gr, with cubic crystal structure and greater solubility in HCl, by slow addition of acetone: Neth. pat. Appl. 6,409,689 (1965 to Upjohn Co.), *C.A.* 63, 5458f (1965). mp 145–147°. [α]$_D^{25}$ +137° (c = 1 in water). No ultraviolet absorption max (220–400 mμ). Freely sol in water, methanol, ethanol; sparingly sol in most organic solvents other than hydrocarbons.

MED USE: Antimicrobial. *Dose:* Oral 500 mg; i.m., i.v. 600 mg. *Side Effects:* G.I. symptoms, pruritus, urticaria may occur.

Lindane. *1,2,3,4,5,6-Hexachlorocyclohexane;* HCH; Viton; *incorrect name:* benzene hexachloride; gamma benzene hexachloride [*not to be confused with hexachlorobenzene*]; Gammexane; Gexane; 666; Ben-Hex; BHC; Aphtiria; Aparasin; Streunex; Tri-6; Lorexane; Kwell; Jacutin. C$_6$H$_6$Cl$_6$; mol wt 290.85. C 24.78%, H 2.08%, Cl 73.14%. Eight well-described stereoisomers. The gamma isomer is the effective insecticide, hence the names Gammexane, Gexane, etc. The early technical mixture, prepd by the chlorination of benzene in the presence of light, contained about 12% of the γ-isomer and about 12% of the β-isomer, large amounts of the α-isomer were also present. Prepns sold for pharmaceutical or medicinal purposes now contain at least 99% pure γ-isomer as the active ingredient. The *cis-trans* relationships of the Cl substituents in the different isomers are: α = 1,2,4/3,5,6; β = 1,3,5/2,4,6; γ = 1,2,4,5/ 3,6; δ = 1,2,3,5/4,6; ε = 1,2,3/4,5,6; ζ = 1,2,3,4,5,6; η = 1,2,3,4/5,6; θ = 1,2,3,4,5/6. Prepn: Gunther, *Chemistry & Industry (London)* 1946, 399; U.S. pat. 2,218,148 (1940 to I.C.I.). Nomenclature and structure: Hornstein, *Science* 121, 206 (1955).
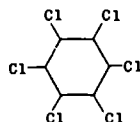
α-Isomer: crystals from alcohol. Persistent acrid odor. mp 158°. Vapor press. 0.06 mm Hg at 40°. Volatile with steam. Insoluble in water. Soluble in 22.8 parts chloroform at 15.25°; in 15.4 parts benzene at 18.25°.

β-Isomer: crystals from alcohol. mp 312°. Sublimes after melting. Not volatile with steam. Vapor press 0.17 mm Hg at 40°. Soluble in 775 parts chloroform at 20°; in 213 parts benzene at 17.25°.

γ-Isomer: crystals, mp 112.5°. Slight musty odor. Vapor press. 0.14 mm Hg at 40°. Soluble in 13.5 parts chloroform at 20°, in 19 parts abs alcohol, in 2 parts acetone, in 5.5 parts ether, in 3 parts benzene. Insoluble in water.

USE: Insecticide.

Third column

MED USE: Scabicide, pediculicide. *Dose:* Topically 1% lotion or cream. *Human Toxicity:* Poisoning may occur by ingestion, inhalation, or percutaneous absorption. *Acute:* dizziness, headache, nausea, vomiting, diarrhea, tremors, weakness, convulsions, dyspnea, cyanosis, circulatory collapse. Estimated fatal oral dose 150 mg/kg body wt. *Chronic:* hepatic damage has occurred in exptl animals. Topical use may cause local sensitivity reactions. Vapors may irritate eyes, nose, throat. *Caution:* Avoid prolonged or repeated applications.

VET USE: Parasiticide for ectoparasites.

Linnaeite. Co$_3$S$_4$—cobalt sulfide.

Linoleic Acid. *cis-9,cis-12-Octadecadienoic acid;* 9,12-linoleic acid; linolic acid. C$_{18}$H$_{32}$O$_2$; mol wt 280.44. C 77.09%, H 11.50%, O 11.41%. An essential fatty acid, component of vitamin F. Major constituent of many vegetable oils, *e.g.,* cottonseed, soybean, peanut, corn, sunflowerseed, safflowerseed, poppyseed, linseed, and perilla oils, where it occurs as a glyceride. Characteristic ingredient of semi-drying oils. Isoln: Swern, Parker, *J. Am. Oil Chemists' Soc.* 30, 5 (1953); Parker *et al., Biochem. Prepns.* 4, 86 (1955); McCutcheon, *Org. Syn.* coll. vol. III, 526 (1955). Summary of work on structure: T. P. Hilditch, *The Chemical Constitution of Natural Fats* (Chapman & Hall, London, 2nd ed 1956). Synthesis: Raphael, Sondheimer, *J. Chem. Soc.* 1950, 2102; Gensler, Thomas, *J. Am. Chem. Soc.* 73, 4601 (1951); Walborsky *et al., ibid.* 2590; Nigam, Weedon, *J. Chem. Soc.* 1956, 4052; Osbond, Wickens, *Chemistry & Industry (London)* 1959, 1288.
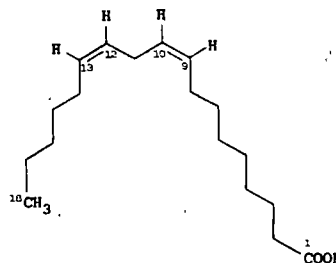
Colorless oil. Easily oxidized by air, cannot be distilled without decompn. Storage in ester form is recommended. d$_4^{18}$ 0.9038; d$_4^{22}$ 0.9007. mp −12°. bp$_{1.4}$ 202°; bp$_{16}$ 230°. $n_D^{11.5}$ 1.4715; n_D^{20} 1.4699; $n_D^{21.5}$ 1.4683; n_D^{60} 1.4588. Iodine value: 181.1. Thiocyanogen value 96.7. Freely sol in ether. Soluble in abs alc. One ml dissolves in 10 ml petr ether. Miscible with dimethylformamide, fat solvents, oils.

Aluminum salt, Al(C$_{18}$H$_{29}$O$_2$)$_3$. Yellow lumps or powder; linseed oil odor. Practically insol in water; sol in oils, fixed alkali hydroxides.

Methyl Ester see Methyl Linoleate.

Ethyl Ester *see* Ethyl Linoleate.

USE: Manuf paints, coatings, emulsifiers, vitamins. Aluminum salt used to manuf lacquers.

MED USE: Essential nutrient. *Human Toxicity:* No systemic toxicity. Locally can cause mild irritation. Large doses orally can cause nausea and vomiting.

Linolenic Acid. *9,12,15-Octadecatrienoic acid.* CH$_3$(CH$_2$CH═CH)$_3$CH$_2$(CH$_2$)$_6$COOH; mol wt 278.42. C$_{18}$H$_{30}$O$_2$; C 77.65%, H 10.86%, O 11.49%. Occurs as the glyceride in most drying oils. Synthesis: Nigam, Weedon, *J. Chem. Soc.* 1956, 4049; Osbond, Wickens, *Chemistry & Industry (London)* 1959, 1288.

Colorless liquid. d$_4^{18}$ 0.914. bp$_1$ 230–232°. Insoluble in water; sol in organic solvents.

MED USE: Dietary supplement.

Linseed. Flaxseed; linum. Dried ripe seeds of *Linum usitatissimum* L., *Linaceae.* Source of linseed oil. *Constit.* 30–40% oil, about 6% mucilage, about 25% proteins and linamarin.

MED USE: Topical demulcent, emollient.

VET USE: The crushed seeds were formerly used as a poultice.

Linseed Oil. The oil obtained by expression of linseed. *Constit.* Glycerides of linolenic, linoleic, oleic, stearic,

Fourth column (partial)

palmitic and myristic
ical Constitution of
p 175 sqq. E. W. Ecl
1954), pp 535–547.

Yellowish liq, pec
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Iodine no. not belov
1.5%. Slightly sol
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USE: In varnishe
printing inks, artific
enameling leather; ;
them waterproof anc
MED USE: Emollie
VET USE: Laxative
500–750 ml; sheep
suitable for small an.

Linseed Oil, Sulf
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Brownish-red visc:

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form, such as glycer
Catalyzes digestion.
also in molds, bact
animal tissues, espec
beans: H. Gibian in
Chemie, 3rd ed, **vol.**

The optimum ten
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USE: To split fats
such as vitamins or
MED USE: Digestiv

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Rev. 12, 241 (1960).
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reduction of the o
Warren, *Chem. Ne*
2,028,390 (1936).

♦EPA

Ambient
Water Quality
Criteria for
Hexachlorocyclohexane
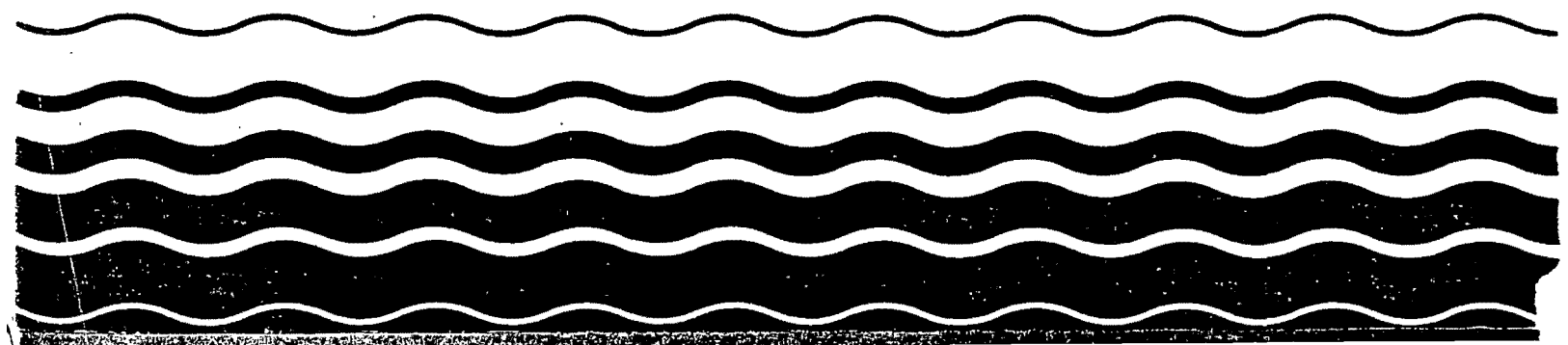
INTRODUCTION

Hexachlorocyclohexane is a broad spectrum insecticide of the group of cyclic chlorinated hydrocarbons called organochlorine insecticides. It consists of a mixture of five configurational isomers and was introduced in 1942 as a contact insecticide under the trade names BHC, benzene hexachloride, and 666. Since its introduction, both the used and production volume of technical grade BHC have undergone dramatic changes as a result of the discovery that virtually all of the insecticidal activity of BHC resides with its γ-isomer. By voluntary action, the principal domestic producer of technical grade BHC requested cancellations of its BHC registrations on September 1, 1976. As of July 21, 1978 all registrants of pesticide products containing BHC voluntarily cancelled their registrations or switched their former BHC products to lindane formulations. On the other hand, significant commercial use of the purified γ-isomer of BHC (lindane) continues. As of January 17, 1977, there were 557 Federal registrations for pesticide products containing lindane and 87 formerly State-registered products containing lindane for which Federal registration has been requested.

Hexachlorocyclohexane, commonly referred to as BHC or benzene hexachloride, is a brownish-to-white crystalline solid with a phosgene-like odor, a molecular formula of $C_6H_6Cl_6$, a molecular weight of 290.0, a melting point of 65°C, and a solubility in water of 10 to 32 mg/l (Hardie, 1972; Clristensen, 1976; Matsumura, 1975). BHC is the common name approved by the International Standards Organization for the mixed configurational isomers of 1,2,3,4,5,6-hexachlorocyclohexane, although the terms BHC and benzene hexachloride are misnomers for this aliphatic compound and should not be confused with aromatic compounds of similar structure, such as the aromatic

compound hexachlorobenzene (Int. Agency Res. Cancer, 1974). Lindane is the common name approved by the International Standards Organization for the γ-isomer of 1,2,3,4,5,6-hexachlorocyclohexane. BHC is synthesized by the direct action of chlorine on benzene in the presence of ultraviolet light (Hardie, 1972).

Technical grade BHC contains the hexachlorocyclohexane isomers in the following ranges: α-isomer, 55 to 70 percent; β-isomer, 6 to 8 percent; γ-isomer, 10 to 18 percent; δ-isomer, 3 to 4 percent; ϵ-isomer, trace amounts (Hardie, 1972). The actual content of the isomers in technical grade BHC varies depending on the manufacturing conditions.

In addition to the hexachlorocyclohexane isomers, technical grade BHC may contain varying quantities (three to five percent) of other chlorinated derivatives of cyclohexane primarily heptachlorocyclohexane and octachlorocyclohexane.

Technical grade BHC is available in various formulations as wettable powders, granules, dusts, and emulsifiable concentrates and can be used as a stomach and contact poison for a wide variety of insect pests and animal parasites. Since the γ-isomer (lindane) has been shown to be the insecticidally active ingredient in technical grade BHC (Hardie, 1972), technical grade BHC now has limited use commercially except as the raw material from which the purified γ-isomer is extracted by a process of selective crystallization.

Technical grade lindane is composed of 99 to 100 percent pure γ-BHC isomer and is available in the form of emulsifiable concentrates, wettable powders, dusts, crystals, and solids for smoke generators and thermal vaporizers.

The physical properties of the purified BHC isomers are presented in Table 1.

TABLE 1

Physical Properties of BHC Isomers*

BHC Isomer	Melting Point (°C)	Vapor Pressure (mm Hg at 50°C)	Water Solubility (mg/l)	Solubility in Relatively Non-polar Solvent (g/100 g ether at 20°C)
alpha	158	0.00087	10	6.2
beta	312	0.000014	5	1.8
gamma	112.5	0.0008	10	20.8
delta	138	---	10	35.4

*Source: Hardie, 1972; Ulmann, 1972

The isomers of BHC are not susceptible to photolysis or strong acids but are, with the exception of the β-isomer, dehydrochlorinated by alkalies to form primarily 1,2,4-trichlorobenzene (Hardie, 1972). Lindane has been shown to be slowly degraded (ten percent degradation after six weeks) by soil microorganisms (Mathur and Saha, 1975) and is capable of isomerization to α- and/or δ-BHC by microorganisms and plants (Matsumura, et al. 1976; Newland, et al. 1969; Steinwandeter, 1976).

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CHLOROSULFURIC ACID

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35. *Synthetic Organic Chemicals, United States Production and Sales*, United States International Trade Commission, Washington, D.C., 1960–1978.
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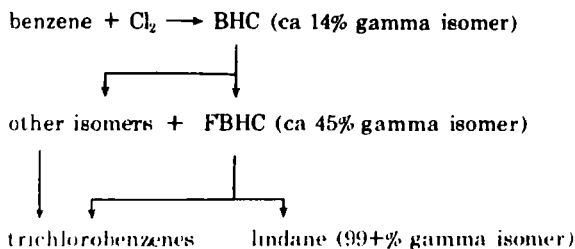37. *British Intelligence Objectives Subcommittee*, 986, 151.

CHE-I KAO
NOLAND POFFENBERGER
Dow Chemical U.S.A.

BENZENE HEXACHLORIDE

Benzene hexachloride [608-73-1], (1,2,3,4,5,6-Hexachlorocyclohexane, Agrocide, Ambiocide, Benzanex, Benzex, BHC, Gammacide, Gammacoid, Gamaspra, Gamtox, Gyben, Hexachlorane, HCH, Hexdow, Isatox, Lintox, Lexone, Trives-T), a mixture having a high level of insecticidal activity, is the fully saturated product formed by light catalyzed addition of chlorine to benzene. This reaction produces a number of stereoisomeric compounds of the composition $C_6H_6Cl_6$, with varying amounts of both underchlorinated and overchlorinated compositions. This mixture, commonly called BHC, is one of the major families of chlorohydrocarbon insecticides (see Insect control technology).

The benzene hexachloride mixture is no longer used commercially in the United States. It is processed primarily either to provide a product with increased content of the gamma isomer or to provide the pure gamma isomer, commonly called lindane. It is the only isomer with significant insecticidal activity. In warm blooded animals important differences in pharmacological effects exist between isomers, eg, the alpha and gamma isomers are central nervous system depressants (1). Excellent sources of activity information are reported in refs. 2 and 3.

The benzene hexachloride mixture containing about 14% gamma isomer is a brown-to-white amorphous powder with a musty odor reminiscent of the new-mown-hay odor of phosgene. This mixture is processed by selective crystallization to a crystalline solid containing 40–48% gamma isomer. This product, called Fortified Benzene Hexachloride (FBHC), is no longer used in the United States but is still produced and sold internationally as an insecticide, or as a raw material for production of lindane (Gamma BHC, Gamaphex, Gammalin, Gammex, Gammexane, Jacutin, Lindafor, Lindagam, Lintox, Novigam, Silvanol, and Gamma HCH). The latter compound is a crystalline free-flowing solid containing 99+% gamma isomer showing high activity in a wide variety of insects.

benzene + Cl₂ ⟶ BHC (ca 14% gamma isomer)

other isomers + FBHC (ca 45% gamma isomer)

trichlorobenzenes   lindane (99+% gamma isomer)

The undesired isomers remaining are often thermally treated to produce tri-chlorobenzenes.

Benzene hexachloride was first prepared by Faraday in 1825 by the addition of chlorine and benzene in sunlight. In 1833 Mitscherlich demonstrated important structural information by the dehydrochlorination of crude BHC with alkali to form trichlorobenzenes. In 1884 Meunier isolated the first two isomers alpha and beta, but gave no indication of their structures. Van der Linden in 1912 isolated the former as well as the gamma (lindane) and delta isomers. He concluded that the four isomers then known resulted from distribution of hydrogen and chlorine atoms either above or below the plane six-membered ring. The epsilon isomer was detected in 1947 (4). The eta and theta isomers were detected from the photochlorination of benzene tet-rachloride (5). Identification of the final member of the series, the iota isomer, was claimed in 1969 (6), but as yet no definitive structure proof has been completed.

The insecticidal activity of BHC against the Colorado beetle was first noted in 1940 (7). In a search for an alternative to the expensive rotenone, ICI in 1942 discovered that the gamma isomer of BHC was active against grain weevils, the turnip flea beetle and other insects (8). Large quantities of BHC were used during World War II under the name Aphtiria.

Physical Properties

Structure of the Benzene Hexachloride Isomers. The misnomer benzene hexa-chloride has been associated with the stereoisomers of 1,2,3,4,5,6-hexachlorocyclo-hexane (9).

Although slightly imprecise, the conformational isomers are called chair and boat forms in this article. Terms such as half chair, skew boat, distorted torsion angles, etc, are more precise but add little to this level of understanding. Crystallographic structure determinations and nmr studies have given thorough structural details (10–13).

The stereoisomer least likely to interconvert will be the one with three or more chlorines in equatorial positions. The following shows chair–chair interconversion:
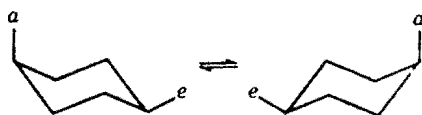
where a = axial; e = equatorial.

There are sixteen theoretical isomers. Chair–chair interconversions reduce this number to eight. The favorable conformations (bold-face) have three or more equa-torial chlorines.
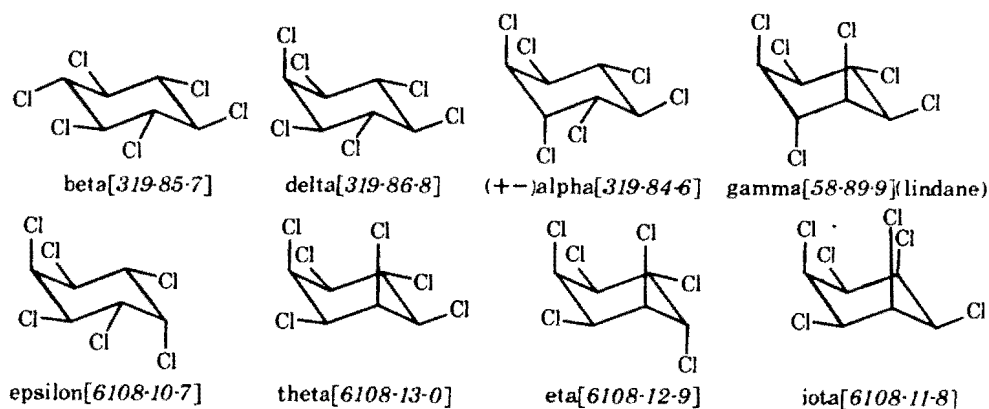
e e e e e e $\rightleftharpoons$ $a a a a a a$	beta isomer
a e e e e e $\rightleftharpoons$ $e a a a a a$	delta isomer
a a e e e e $\rightleftharpoons$ $e e a a a a$	alpha isomer
a e a e e e $\rightleftharpoons$ $e a e a a a$	theta isomer
a e e a e e $\rightleftharpoons$ $e a a e a a$	epsilon isomer
a a a e e e $\rightleftharpoons$ **e e e a a a**	gamma isomer
a a e a e e $\rightleftharpoons$ **e e a e a a**	eta isomer
a e a e a e $\rightleftharpoons$ **e a e a e a**	iota isomer

Of the eight isomers only alpha and eta are enantiomorphs. The eta isomer, on chair-chair interconversion, becomes superimposable on its mirror image. Therefore,

only the alpha isomer is optically active. The *levo* enantiomer of the alpha isomer has been isolated by reaction of racemic modification of the alpha isomer with the optically active alkaloid brucine (14). The subsequent dehydrochlorination to trichlorobenzene only occurred with one enantiomer and not the other.

Analytical and structural determinations have validated the structures of five of the isomers (10–13).

The accepted structures for the eight isomers of benzene hexachloride are shown below.

beta[319-85-7]   delta[319-86-8]   (+ –)alpha[319-84-6]   gamma[58-89-9](lindane)

epsilon[6108-10-7]   theta[6108-13-0]   eta[6108-12-9]   iota[6108-11-8]

The structure–activity relationship for the insecticidal activity of the gamma isomer has yet to be explained. An interesting observation is that the gamma isomer is the only BHC stereoisomer which is known to sustain chair–chair interconversion at ambient temperature (the nmr spectrum is a single sharp line showing equivalence of all hydrogens at room temperature), and has the largest spherical volume of any of the common isomers. A volume–activity correlation has been suggested (14). Others have tried to relate the toxicity of the gamma isomer to DDT (15) since the effect on insects is similar and the dimensions of both are similar. Many isosteres of the gamma isomer have been prepared with alkyl, methoxy, or halo substituents. These showed activity less than lindane but did relate to hydrophobic–lipophilic properties of the substituents. All isosteres provoked central nervous system changes.

Technical BHC. Technical BHC is a brownish-to-white solid having a musty odor which melts around 63°C. It can be distilled with no decomposition. The composition of the various isomers in benzene hexachloride depends on conditions of manufacture but is commonly as follows:

Isomer	%
α	65
β	7
γ	14
ϵ	4
others	10
Total	100

The principal reported physical constants of the five major isomers are shown in Tables 1 and 2.

Solubilities of the benzene hexachloride isomers in several organic solvents are shown in Table 2.

Table 1. Comparison of the Physical Constants of Lindane and Some of the Other BHC Isomers[a]

Isomer	Isomer in technical BHC, %	mp, °C	Dipole moment $C \cdot m \times 10^{-30b}$	Refractive index, n_D^{20}	λ_{max}, nm	Crystal
α	55–70	159.2	7.41	1.626	125.8	monoclinic prisms
β	5–14	311.7	0	1.633	134.6	cubic (octahedral)
γ	10–18	112.9	6.0:12.0	1.644	132.2	monoclinic plates, prisms
δ	6–10	140.8	7.34	1.576–1.674	118.1	fine plates
ε	3–4	218.2	0	1.635	139.6	monoclinic needles or hexagonal monoclinic crystals

[a] Ref. 16.
[b] To convert C·m to debye, divide by 3.336×10^{-30}.

Table 2. Solubility of the Various Isomers at 20°C, in g/100 g Solvent[a]

Solvent	Alpha	Beta	Lindane (ca 100% gamma)	Delta	Epsilon
ethyl acetate	12.7	6.9	35.7	58.5	
acetone	13.9	10.3	43.5	71.1	33.2
acetic acid	4.2	1	12.8	25.6	
ethyl alcohol	1.8	1.1	6.4	24.2	4.2
benzene	9.9	1.9	28.9	41.1	
chloroform	6.3	0.3	24.0	13.7	2
dioxane	33.6	7.8	31.4	58.9	
ether	6.2	1.8	20.8	35.4	3
carbon tetrachloride	1.8	0.3	6.7	3.6	0.5
toluene	9	2.1	27.6	41.6	

[a] Ref. 17.

The odor of BHC has been attributed to both under- and over-chlorinated cyclohexanes as well as chlorocyclohexenes. Many schemes have been proposed for odor removal but a simple carbon treatment (18) appears easiest. The pure gamma isomer retains only a very faint odor.

Fortified BHC. Fortified Benzene Hexachloride (FBHC) is a brown-to-white solid which melts near 78°C. The composition of the various isomers in FBHC depends on manufacture but is commonly as follows:

Isomer	%
α	19
β	10
δ	21
γ	44
ε	1
others	15

Lindane. Lindane is a crystalline white free flowing solid, 99+% gamma isomer which melts at 112°C. The pure gamma isomer has three modifications, one rhombic, and two monoclinic which are enantiotropic to the rhombic form. The melting points of the two stable forms are very close together. These isomers are relatively stable

chemically and do not lose hydrogen chloride when heated with traces of metals and their salts. They are also stable to light and oxidative conditions.

Chemical Properties

With the exception of the β isomer, the isomers of BHC are dehydrochlorinated by alkali at 60°C to give primarily 1,2,4-trichlorobenzene. This is formed largely from the alpha isomer (60–80%). The γ and δ isomers, in addition, yield lesser quantities of 1,2,3- and 1,3,5-trichlorobenzenes. Cristol (19) showed that in the case of the α and γ isomers the dehydrochlorination takes place by a simple second-order reaction, whereas the reaction of the δ isomer is kinetically more complex. Less stringent reaction conditions give chlorinated cyclohexenes.

When BHC is chlorinated in carbon tetrachloride, various substitution derivatives are formed. By use of liquid chlorine, higher substituted derivatives can be obtained (20–21). BHC vapor in admixture with oxygen (air) and chlorine at 470°C in the presence of a catalyst containing alumina, copper chloride, and potassium chloride yields a mixture of hexachlorobenzene and pentachlorobenzene (22). High temperature chlorination in a chlorobenzene solvent in the presence of ferric chloride also results in the quantitative conversion of BHC to hexachlorobenzene (23).

BHC reacts readily with sulfur at 240–290°C, with elimination of two chlorine atoms and formation of a sulfur link between two pentachloro residues (24):
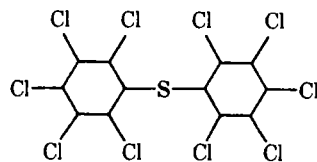
This derivative, known as SPC (Sulphure de Polychlorocyclane), has found some application in Europe as a pest control agent.

With elementary sulfur at 240–290°C, p-dichlorobenzene and 1,2,4,5-tetrachlorobenzene are formed with evolution of hydrochloric acid, sulfur dichloride, and hydrogen sulfide. Small quantities of 1,2,3- and 1,3,5-trichlorobenzenes are also produced (25).

Analysis of products of tritiated gamma isomer showed that tritiation occurs with dechlorination, and retention or inversion of the steric conformation, and the resulting pentachlorocyclohexane is labeled at the dechlorinated position (26).

Boiling water or steam treatment of BHC liberates only traces of hydrochloric acid, but at 200°C in sealed tubes 1,2,4-trichlorobenzene is formed. To inhibit decomposition, BHC is stored for long times at temperatures above ambient with added 1% sodium thiosulfate.

Treatment of BHC with zinc dust in acids dechlorinates the material to benzene. Although generally inert to strong acids, BHC is decomposed to benzene by chlorosulfonic acid or sulfur trioxide.

chloral?

Manufacture

Technical benzene hexachloride is produced by the addition-chlorination of benzene in the presence of free radical initiators such as visible or ultraviolet light, x-rays, or gamma rays.

The only reported kinetic studies of the photochemical chlorination of benzene were carried on in the vapor phase (27).

There is probably a secondary substitution process occurring since chlorobenzene and both hepta- and octachlorocyclohexane appear in small amounts under most experimental and production conditions.

Technical benzene hexachloride is produced by either batch or continuous methods in either stirred tank type reactors or tubular reactors. In a typical process, benzene is chlorinated at 15–25°C in a glass reactor at 101 kPa (1 atm) with excess benzene. It is necessary to exclude oxygen and substitution catalysts, eg, iron. When ca 5–8% benzene is chlorinated (measured commonly by specific gravity), the beta isomer begins to precipitate. Benzene and excess chlorine are removed by evaporation at 85–88°C. If the desired product is to be what is commonly called technical benzene hexachloride, part of the benzene is removed first by evaporation at ambient pressure. Residual benzene is stripped at reduced pressure. Recovered benzene is condensed, scrubbed and returned to the reactor. The molten product is steam-stripped to remove traces of benzene and then cast into shallow pans. The gamma content of a typical product is 12–14%.

The gamma-isomer content can be increased significantly by the reaction of benzene and chlorine in a nonreactive solvent of high dielectric constant such as methylene chloride (27–28). In these solvents, gamma isomer contents as high as 26% have been reported. There are many reported variants of the above process for obtaining a higher gamma-isomer content (29–30).

Since the gamma isomer is more soluble than the alpha or beta isomers in most common solvents, including benzene, enrichment of gamma isomer is obtained by crystallization of the less soluble isomers in the region of gamma saturation. The solid phase of alpha and beta isomers can then be separated by filtration or centrifugation. The concentration of the gamma isomer in the solution phase will depend on the solvent used. For most producers the solvent used is benzene, giving a concentrate containing 40–45% of the gamma isomer. With other solvents, such as chlorinated hydrocarbons, a gamma content as high at 60% may be obtained through these extraction methods. The concentrate, known commercially as fortified BHC (FBHC), contains all the gamma, delta, and epsilon isomers present in the original crude benzene hexachloride, as well as minor amounts of hepta- and octachlorocyclohexanes and residual alpha and beta isomers. This mixture has a low and indistinct crystallization temperature. The melt can be supercooled to room temperature without inducing crystallization. Once solidified, the last crystal point is in the region of 70–80°C.

No commercial process has yet been found which permits recovery of all of the gamma isomer present in crude benzene hexachloride. Because of these inevitable losses and the attendant processing costs, some of the gamma isomer is marketed as technical BHC. However, there are many applications for which the undesirable properties of this crude material, such as the musty, acrid odor, and phytotoxicity of some isomers, are sufficiently objectionable to warrant the premium price of the purified material. Household and home garden formulations, seed treatment, etc, are

made with lindane for these reasons. Lindane is the only BHC composition sold in the United States.

Numerous procedures have been described and patented for isolation of the highly desired gamma isomer (31–32). Only two of these procedures are known to be used commerically for lindane preparation: the supersaturation process, and the fluid classification process. Intermediate steps in concentrating the gamma isomer may employ one or more of the other procedures, however, before carrying out the primary stage of isolating the gamma isomer.

The usual solvent for the supersaturation process is a lower primary alcohol, generally methanol. Alcohol–water systems are also described in several patents. An appreciable portion of the gamma isomer is left in the concentrate when the limit of supersaturation of alpha isomer is reached. Further recovery of gamma isomer can be obtained by removal of the alcohol solvent and crystallization of a gamma-rich concentrate from a solvent having very different solubility characteristics for the various isomers such as carbon tetrachloride or a paraffinic hydrocarbon.

Preparation of lindane by the supersaturation process requires recovery of the gamma isomer from a solution containing a high concentration of impurities. Final purification of the resultant lindane is troublesome, and trace impurities are difficult to eliminate. If mixed crystals are obtained by crystallization from solution of alpha, beta, and gamma isomers, the very small alpha and beta crystals (33) can be separated from the gamma crystals by decanting a suspension of the smaller particles.

The delta isomer and minor soluble impurities are first separated from the alpha, beta, and gamma isomers by preparation of a saturated solution of the gamma isomer in an alcoholic solvent. Alcohols, eg, methanol or isopropanol, are very effective for this separation and also yield excellent crystal forms for subsequent crystal classification. An extremely pure lindane is obtained by this process, which accounts for virtually all of the production in the United States.

Although interest in new BHC–FBHC–lindane production methods has been limited in recent years, it has by no means disappeared. A scheme has been patented that provides for integrated production of lindane with full recovery of HCl and trichlorobenzenes (34). In addition, a mathematical model of stream structure has been proposed for a methanol extraction apparatus for production of enriched hexachlorocyclohexane (35).

Economic Aspects

Commercial production was begun by Hooker Chemical Corporation in the United States in early 1946. New producers were announced almost monthly until, by 1951, sixteen United States manufacturers released a flood of 53,000 metric tons of benzene hexachloride in various forms, equivalent to ca 8200 t of gamma isomer. The market was able to absorb only 60% of this output and production in subsequent years declined steadily to reach a fairly stable level of ca 2000 t/yr of the gamma isomer in all forms by 1960. This output was supplied by five domestic producers with a reported productive capacity about twice that of current market requirements. This oversupply became apparent and slowly producers dropped out of production.

During the 1960s and 1970s the toxic effects of the undesired isomers became known. As a result, by 1977 there was only one United States producer of lindane. The 1977 sales price was $7.72/kg.

World consumption of BHC and lindane (in metric tons) was:

Year	BHC	Lindane
1970	42,000	16,000
1971	28,000	13,000
1972	25,000	12,000
1973	30,000	8,000
1974	25,000	4,000

There is still activity in this field, eg, there is a new lindane–BHC facility capable of producing 11,000 t/yr in Spain (36).

The general prognosis for BHC is a fast decline in developed countries with a slow decline in developing countries where the lower prices are attractive. The situation is similar for FBHC.

Analytical Methods

There are no definitive chemical tests for the presence of any of the isomers of benzene hexachloride since they are all isomeric. Except for the beta isomer, they are similar in reactivity.

Although many analytical methods have been used for analysis of these isomers, there are only two that are significant in terms of time of analysis and accuracy. The ir method (37) is nondestructive and repeatable but, because of interferences from overchlorinated materials, its accuracy is suspect. The gas chromatography methods (38–39) are of similar repeatability (±1%). Degradation of the delta isomer occurs when conditions are not carefully maintained. Accurate determination of the minor isomers can be obtained by use of internal standards.

Thin layer chromatography has been used for the qualitative analysis of benzenehexachloride components (7). The analysis is quick and semiquantitative. By use of micro-thin layer chromatography detection levels of 0.025 μg of the individual isomers were observed.

Lindane itself can be estimated either by reaction with o-toluidine followed by measurement of the absorbance in a water/2-butanol mixture containing 0.22% ammonium molybdate (40) or by a similar sequence using ethanolamine in the presence of 0.1% p-nitrobenzenediazonium fluoborate (41).

Health and Safety Factors (Toxicology)

Many of the reports of the toxicology of BHC–FBHC–lindane are contradictory or plagued by experimental protocols using contaminated materials and controls. In the case of BHC–FBHC, the isomer content is extremely variable or not reported at all.

At the liver, hydroxylating enzymes act to make the isomer more polar (as an alcohol or phenol) for secretion as a sulfate or glucosiduronide. All BHC isomers can undergo this fate either directly or after HCl elimination, except the beta isomer which is difficult to eliminate. The more easily an isomer can assume an aromatic nature by HCl evolution, the more easily it can be hydroxylated and subsequently eliminated.

Much of the recent work has been attempted on lindane (2). Most of the following refers to this isomer since it is the active ingredient, and has none of the objectionable beta isomer.

Lindane is used as an insecticide in crop protection, and also as a therapeutic agent in human and veterinary medicine. Its manufacture and its practical application for a period of more than 20 years yield a wealth of experience which together with results of experiments in animals provide the basis for this information on toxicology.

After intake of relatively high quantities either in single or repeated dosage, lindane is fully excreted from the animal body within a short time, ie, ca one day.With repeated application an equilibrium is quickly established between intake and excretion. After cessation of medication the residues which prevail, mainly in body fat, are completely eliminated within days or a few weeks. When present at high levels in the tissues, lindane like a great number of other therapeutic agents stimulates a greater activity of the microsomal enzymes of the liver, and thereby its own metabolism and excretion are enhanced. Residues found in foods reaching the consumer, however, lie well below the threshold value required to produce this effect in experimental animals.

As apparent from the toxicity data given in Table 3, lindane can be classified as a chemical of intermediate acute toxicity. In long-term feeding experiments it shows a much higher no-effect dose value than other chlorinated hydrocarbons, which places lindane in a special position within this group. Even the reversible liver alterations known as chlorinated hydrocarbon liver are not considered to be of pathological character but of an adaptive nature. They need not be taken into consideration when fixing the no-effect level for lindane. The no-effect dosage for rats and dogs in two year feeding studies with lindane was 1.25 mg/kg. The acceptable daily intake (ADI) of 0.0125 mg/kg for man, as tentatively proposed by FAO/WHO has, in comparison with market basket analysis data, a safety factor of ca 100 over the no-effect level (actually, a factor of as much as 2000–4000 over the no-effect dose from animal experiments). Lindane residues are practically of no hygienic importance for the consumer. The real problem in connection with lindane is, however, the past and continued use of technical BHC, from which lindane is produced. Technical BHC used in plant protection and other fields of pest control not only confers taint and off-flavor to foods of plant and animal origin, but produces considerable residues, especially of the alpha and beta isomers, which create hygienic problems. These residues of alpha- and beta-BHC are carried on in the food chain and therefore use of technical BHC should be discouraged.

Other tests with mice, rats, and rabbits have shown that lindane has no teratogenetic effect. A three-generation test with rats proved that fertility as well as survival and development of the young were in no way impaired. In the dominant lethal test and in the host-mediated assay no indications of a mutagenic effect in warm-blooded

Table 3.   Acute Toxicity (LD_{50}) and No-Effect Levels of Some Chlorinated Hydrocarbon Pesticides for Rats[a]

	Lindane (γ-BHC)	Technical BHC	α-BHC	β-BHC	Technical DDT	Chlordane	Heptachlor	Aldrin	Dieldrin	Endrin
oral LD_{50}, mg/kg of body weight	125	600	500	>6000	250	450	90	67	87	7–43
no-effect level from 2-yr feeding tests, ppm in the food	25–50	10	10	<10	1	<2.5	<1	<1	<1	1

[a] Refs 42–44.

animals were apparent for lindane. This was also verified for man by showing no chromosomal changes even after many years of production experience.

Investigations on the oncogenicity of lindane in mice and rats have shown that neoplasms—typical rodent hepatoma—have occurred only in mice and that there is no effect for a 100–300-ppm level of lindane in the daily diet. This effect-level is much higher than that for alpha-BHC or the technical material.

During manufacture and also in the case of pest control operators, strict adherence to industrial hygiene requirements must be observed. It is particularly necessary to ensure the MAC (minimum acceptable concentration) value is not exceeded (0.05 mg/m^3). Increased concentrations in the air are most likely to occur under conditions of poor ventilation and high ambient temperatures which will increase the vaporization of γ-BHC. If factory hygiene principles are properly observed, there is no danger to production operators even with long periods of employment and exposure (see Industrial hygiene and toxicology). Lindane does not have a dangerous accumulative effect and therefore falls outside the classification of persistent chlorinated carbon pesticides (see Trace and residue analysis).

Residues of lindane in warmblooded animals and birds and other vertebrates are in general low and do not constitute a hazard to terrestrial wildlife. Levels of lindane in surface waters are in general in the order μg/L (ppb) and thus below the critical level for fish and other water organisms. Under practical field conditions lindane is generally of low phytotoxicity.

Uses

Lindane as one of the oldest chlorinated insecticides has generated many uses. A list covering 200 pages is available in the monograph *Lindane* (2). The fields of use discussed are: field crops, vegetable crops, fruit crops, viticulture, ornamentals, pasture and forage crops, forestry, soil treatment, seed treatment (seed dressing), locust control. timber protection (termite and ant control), stored materials and products, agricultural and industrial stores, public health, and veterinary hygiene).

No significant use apart from those due to its biological properties have been observed.

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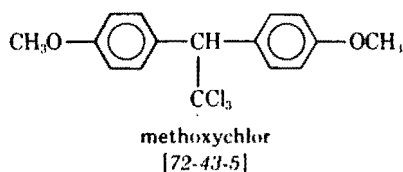# CHEMICAL TECHNOLOGY

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HYDROGEN-ION ACTIVITY
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LAMINATED MATERIALS, GLASS

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                |
               CCl₃

methoxychlor
[72-43-5]

DDT does and is favored for general environmental use. Unfortunately, however, insects that are resistant to DDT generally are cross-resistant to methoxychlor.

Benzene Hexachloride and Lindane. The active constituent of benzene hexachloride [58-89-9], is γ-1,2,3,4,5,6-hexachlorocyclohexane, or lindane, which has the following structural formula:

lindane
[58-89-9]
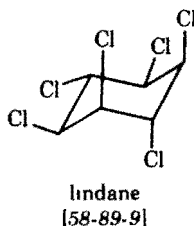
Benzene hexachloride is prepared by the chlorination of benzene in the presence of sunlight. The crude product is a grayish or brownish amorphous solid with a characteristic odor; it begins to melt at 65°C. It consists of 10–18% of the active γ isomer (configuration *aaaeee,* where *a* denotes axial and *e* equatorial) (mp 112°C) with at least four other nearly inactive stereoisomers. α-isomer (*aaeeee* or *aeeeea*) (mp 157°C), 55–70%; β isomer (*eeeeee*) (mp 309°C), 5–14%; δ isomer (*aeeeee*) (mp 138°C, 6–8%); ϵ isomer (*aeeaee*) (mp 219°C), 3–4%; and a trace of η isomer (*aeaaee*) (mp 90°C) (see Chlorocarbons, chlorinated benzenes). A heptachlorocyclohexane is present up to 4% as is a trace of an octachlorocyclohexane; both are insecticidally inactive. The γ isomer is by far the most toxic of the isomers, being from 500–1000 times as active as the α isomer and ca 5000–10,000 times as active as the δ isomer; the β isomer and ϵ isomer are nontoxic. The various isomers differ greatly in their solubilities, and pure γ isomer can be prepared by treating the crude product with methyl alcohol or acetic acid, in which the α and β isomers are nearly insoluble (leaving a marketable product containing 30–40% γ isomer), and then fractionally crystallizing the alcohol-soluble fraction from chloroform or by chromatographic adsorption. The pure γ isomer has a slight aromatic odor (d 1.85 g/cm³; vapor pressure 1.3 mPa (9.4 nm Hg) at 20°C). It is very stable to the action of heat, light, and oxidation and can be burned without appreciable decomposition but readily decomposed by alkaline materials to form, principally, 1,2,4-trichlorobenzene and three moles of hydrogen chloride. The solubilities of the γ isomer (g/100 g of solvent at 20°C) are: acetone, 43; benzene, 29; carbon tetrachloride, 7; cyclohexanone, 37; ethyl acetate, 36; ethyl alcohol, 6; ethylene dichloride, 29; diesel oil, 4; deodorized kerosene, 2; dioxane, 31; mineral oil, 2; xylene, 25; and water, 0.001.

The crude benzene hexachloride has been used extensively as a soil poison, as a toxicant for grasshopper control and against cotton insects. Great care should be exercised in applying benzene hexachloride to edible crops or to soil in which such crops are to be grown, as severe off-flavors of the produce may result. This difficulty has been largely overcome by marketing the 99% pure γ isomer, lindane, for use on food crops, and as a household and public health insecticide. Lindane is of moderate toxicity to mammals with a rat oral and a dermal LD_{50} of ca 100 and 1000 mg/kg, respectively. Its mode of action is unknown but the specific toxicity of the γ isomer suggests that, like DDT, it may interact with the pores of the lipoprotein structure of the insect nerve, thereby causing distortion and consequent excitation of ionic transmission.

Chlorinated Terpenes. A group of incompletely characterized insecticidal compounds has been produced by the chlorination of the naturally occurring terpenes. Toxaphene [8001-35-2] is prepared by the chlorination of the bicyclic terpene, camphene, to contain 67–69% chlorine and has the empirical formula $C_{10}H_{10}Cl_8$. The technical product is a yellowish, semicrystalline gum (mp 65–90°C, d^{25} 1.64 g/m^3) and is a mixture of 175 polychloro derivatives. Toxaphene is unstable in the presence of alkali, upon prolonged exposure to sunlight, and at temperatures above 155°C, liberating hydrogen chloride and losing some of its insecticidal potency. It is very soluble in organic solvents; the solubilities (g/100 mL of solvent) for benzene, carbon tetrachloride, ethylene dichloride, and xylene are >450; for kerosene, 280; and for mineral oil, 55–60; but toxaphene is insoluble in water. The oral LD_{50} to the rat is 69 mg/kg.

The most active ingredients in technical toxaphene are 2,2,5-endo-6-exo-8,9,10-heptachlorobornane [51775-36-1] (mouse ip LD_{50} 6.6 mg/kg); and 2,2,5-endo-6-exo-8,9,9,10-octachlorobornane (mouse ip LD_{50} 3.1 mg/kg). Each constitutes ca 2–6% of the technical mixture.
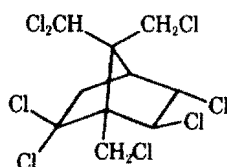
2,2,5-endo-6-exo-8,9,9,10-octachlorobornane
[58002-18-9]

Environmental. Toxaphene is extremely toxic to fish with LC_{50} values to trout and blue gill of 0.003–0.006 ppm. At water concentrations as low as 0.00005 ppm, toxaphene-treated fish suffer broken-back syndrome, a crippling collagen deformity. Bioaccumulation occurs from water to fish at levels up to 100,000-fold. Toxaphene also is highly toxic to birds (oral LD_{50} to pheasant 40 and to mallard 71 mg/kg). The soil persistence of toxaphene is difficult to assess because of the complex mixture but published estimates for half-life range from 2 mo–10 yr. Toxaphene has been found to be a carcinogen in rats and mice. Toxaphene is a broad spectrum, persistent pesticide that is widely used on cotton and other field crops.

Cyclodienes. The cyclodienes are polychlorinated cyclic hydrocarbons with endomethylene-bridged structures, prepared by the Diels-Alder diene reaction. The

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CHLORINATED BENZENES

Twelve chlorinated benzenes can be formed by replacing some or all of the hydrogen atoms of benzene with chlorine atoms.

Physical and Chemical Properties

Table 1 lists some important physical properties.

The chlorine atom in chlorobenzene is sufficiently labile to be hydrolyzed. The hydrolysis of one of the chlorine atoms in 1,2,4,5-tetrachlorobenzene with sodium hydroxide dissolved in a suitable alcohol solvent produces 2,4,5-trichlorophenol. The reaction must be carried out under extremely restricted conditions to prevent the formation of the very toxic compound, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (see Industrial hygiene and toxicology). Nitration of chlorobenzenes with nitric acid has wide industrial applications; however, their uses are declining rapidly.

Manufacture

All chlorobenzenes are now produced by chlorination of benzene in the presence of a Friedel-Crafts catalyst, usually ferric chloride (see Friedel-Crafts reactions). Each compound, except hexachlorobenzene, can be further chlorinated; hence the product is always a mixture of chlorinated benzenes. Pure compounds are obtained by distillation and crystallization. The chlorination reaction is exothermic, liberating heat of ca 1.83 kJ/g Cl_2. Heat is removed in some cases by circulating the reaction liquid through a suitable cooler (see Heat exchange technology); in other cases, chlorination occurs at the boiling point and the heat is removed by the vaporizing liquid.

Benzene chlorination proceeds in a batch, single-, or multistage stirred reactor. The ratio of 1,4- to 1,2-dichlorobenzene varies from 1.4 to 5, depending upon the catalyst. Reactors are subject to design and operating hazards: stagnant areas must be avoided since they allow chlorination to tetra- and pentachlorobenzenes, compounds that cause plugging; spontaneous combustion is a hazard, principally in the vapor phase. Since HCl is present in most parts of the equipment, corrosion is always a potential problem.

Health and Safety

All of the chlorobenzenes are less toxic than benzene. The threshold limit value (TLV) (in ppm per volume of air) for human exposure in 8 h is 50 for 1,2-dichlorobenzene, and 75 for chlorobenzene and 1,4-dichlorobenzene.

Uses

Formerly, large quantities of chlorobenzene had been used in the production of phenol, aniline, diphenyl oxide, and DDT, a widely used

and now restricted insecticide. Monochlorobenzene, 1,2-di- and 1,2,4-trichlorobenzene are used as solvents.

CHE-I KAO
NOLAND POFFENBERGER
Dow Chemical U.S.A.

Chemical Economics Handbook, SRI International, Menlo Park, Calif., 1980.

BENZENE HEXACHLORIDE

Benzene hexachloride, commonly called BHC (1,2,3,4,5,6-hexachlorocyclohexane, Agrocide, Ambiocide, Benzanex, Benzex, Gammacide, Gammaloid, Gamaspra, Gamtox, Gyben, HCH, Hexdow, Isotox, Lintox, Lexone, Trivex-T), is the fully saturated product formed by light-catalyzed addition of chlorine to benzene. This reaction produces a number of stereoisomeric compounds of the composition $C_6H_6Cl_6$, with varying amounts of both under-chlorinated and over-chlorinated compositions. It is used as technical BHC, fortified BHC, or lindane.

Physical Properties

Technical benzene hexachloride (BHC) is a brownish-to-white solid having a musty odor. It melts around 63°C and can be distilled with no decomposition. The composition of the various isomers in benzene hexachloride depends on conditions of manufacture, but is commonly: (mp 159.2°C, n_D^{20} 1.626) 65%; (mp 311.7°C, n_D^{20} 1.626) = 14%; (mp 218.2 C, n_D^{20} 1.635) = 4%; (mp 154.8 C, n_D^{20} 1.576-1.674) = 10%; and traces of others. The odor of BHC has been attributed to both under- and overchlorinated cyclohexanes as well as chlorocyclohexenes and can be removed by a simple carbon treatment.

Fortified benzene hexachloride (FBHC) is a brown-to-white amorphous powder with a musty odor. This mixture is processed by selective crystallization of technical BHC to a crystalline solid containing 40-48% gamma isomer. FBHC melts near 78°C.

Lindane is a crystalline white, free-flowing solid from technical BHC, ≥ 99% gamma isomer. The pure gamma isomer is the only benzene hexachloride isomer with significant insecticidal activity; it has three modifications, one rhombic, and two monoclinic which are enantiotropic to the rhombic form. The melting points of the two stable forms are very close together. These two are relatively heat and chemically stable.

Chemical Properties

With the exception of the beta isomer, the isomers are dehydrochlorinated by alkali at 60°C to give primarily 1,2,4-trichlorobenzene largely from the alpha isomer. The gamma and delta isomers also yield lesser quantities of 1,2,3- and 1,3,5-trichlorobenzenes. When BHC is chlorinated in carbon tetrachloride, various substitution derivatives are formed; use of liquid chlorine yields higher-substituted derivatives. High temperature chlorination in a chlorobenzene solvent in the presence of ferric chloride also results in quantitative conversion of BHC to hexachlorobenzene. BHC reacts readily with sulfur at 240-290°C to form SPC (Sulphure de Polychlorocyclane), used in Europe as a pest-control agent. With elementary sulfur, p-dichlorobenzene and 1,2,4,5-tetrachlorobenzene are formed. To inhibit decomposition, BHC is stored for long times at temperatures above ambient with added 1% sodium thiosulfate. Treatment of BHC with zinc dust in acids dechlorinates the material to benzene. Although generally inert to strong acids, BHC is decomposed to benzene by chlorosulfonic acid or sulfur trioxide.

Manufacture

Technical BHC is produced with a batch or continuous process, in stirred or tubular reactors, by the addition chlorination of benzene in the presence of free-radical initiators such as visible or ultraviolet light, x rays, or gamma rays. A typical method uses reactors at 15-35°C at 101 kPa (1 atm). The gamma-isomer content is significantly increased by the reaction of benzene and chlorine in a nonreactive solvent of high dielectric constant, eg, methylene chloride. No commercial process has yet been found that permits recovery of all of the gamma isomer present in crude benzene hexachloride. Numerous procedures for isolating the highly

Table 1. Physical Properties of Chlorobenzenes

Compound	Mp, °C	Bp 101.3 kPa^a, at °C	Liquid density, g/cm³	Refractive index of liquid, n_D^{25}
chlorobenzene	−45.34	131 7	1.10118	1.5219
1,2-dichlorobenzene	−16.97	180.4	1.3022	1.5492
1,3-dichlorobenzene	−24.76	173.0	1 2828	1.54337
1,4-dichlorobenzene	53.04	174.1	1.2475	1.52849 (55°C)
1,2,3-trichlorobenzene	53.5	218.5		
1,2,4-trichlorobenzene	17.15	213.8	1.44829	1.56933
1,3,5-trichlorobenzene	63.5	208.5		
1,2,3,4-tetrachlorobenzene	46.0	254 9	1.70	
1,2,3,5-tetrachlorobenzene	51	246		
1,2,4,5-tetrachlorobenzene	139.5	248 0	1 83$_{bl}$	
pentachlorobenzene	85	276		
hexachlorobenzene	228 7	319 3	1.596	

^{a} To convert kPa to mm Hg, multiply by 7.5.

desired gamma isomer have been patented; the two used commercially for lindane preparation are the supersaturation process, and the fluid classification process.

Health and Safety

Lindane is of intermediate acute toxicity. BHC used in plant protection produces considerable residues which are carried on in the food chain; use of technical BHC is discouraged.

Uses

Lindane is a broad-spectrum insecticide and selective acaricide with contact and fumigant action. Its primary use in the United States is in seed treatment.

JAMES G. COLSON
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RING-CHLORINATED TOLUENES

The ring-chlorinated derivatives of toluene form a group of stable, colorless compounds. They are prepared directly by chlorination, and indirectly by routes such as reactions involving the replacement of the amino, chlorosulfonyl, hydroxyl, and nitro groups by chlorine, and the use of the sulfonic acid and amino groups to orient substitution followed by their removal from the ring.

Monochlorotoluenes

These are mobile, colorless liquids, miscible in all proportions with many organic liquids such as aliphatic and aromatic hydrocarbons, chlorinated solvents, lower alcohols, ketones, glacial acetic acid, and di-n-butylamine. They are insoluble in water, ethylene, and diethylene glycols, and triethanolamine. o-Chlorotoluene (1-chloro-2-methylbenzene) has mp $-35.6°C$, bp $159.2°C$, and d_{20} 1.083 g/cm^3. p-Chlorotoluene (1-chloro-4-methyl benzene) has mp $7.5°C$, bp $162.4°C$, and d_{20} 1.070 g/cm^3. m-Chlorotoluene (1-chloro-3-methylbenzene) has mp $-47.8°C$, bp $161.7°C$, and d_{20} 1.072 g/cm^3. o- and p-Chlorotoluenes form binary azeotropes with various organic compounds and stable ionic complexes with antimony pentachloride.

Chemical properties. Monochlorotoluenes are stable to the action of steam, alkalies, amines, and hydrochloric and phosphoric acids at moderate temperatures and pressures. Reactions are divided into (*1*) reactions of the aromatic ring, eg, ring chlorination of o-chlorotoluene yields a mixture containing all four possible dichlorotoluene isomers; (2) reactions of the methyl group, which relate to most of the uses of monochlorotoluene products, eg, chlorination under free-radical conditions leads successively to the chlorinated benzyl, benzal, and benzotrichlorides (qv); and (*3*) reactions involving the chlorine substituent, eg, displacement and benzyne mechanisms are involved in the hydrolysis of chlorotoluenes to cresols with aqueous sodium hydroxide.

Preparation. Chlorination of toluene is carried out with a wide variety of chlorinating agents and catalysts and under a variety of reaction conditions. Chlorinations with elemental chlorine yield varying ratios of ortho and para isomers depending on both the chlorinating agent and catalyst used. The para isomer content is of greatest commercial significance. The meta isomer must be prepared by indirect means since only a small amount (usually 1%) is formed by direct chlorination. Pure chlorotoluene isomers (eg, m-chlorotoluene) are available from diazotization of the toluidine isomers followed by reaction with cuprous chloride (Sandmeyer reaction).

Higher Chlorotoluenes

Physical properties of some of the higher chlorotoluenes are listed in Table 1. Of the six dichlorotoluenes, only the 2,4-, 2,5-, and 3,4-isomers

Table I.   Physical Properties of the Higher Chlorotoluenes

Toluene	Mp, °C	Bp, °C	Density at 20°C, g/cm^3
2,4-dichloro	−13.5	201.1	1.250
2,6-dichloro		200.6	1.269
3,4-dichloro	−15.3	208.9	1.256
2,3,4-trichloro	43–44	244	
2,4,5-trichloro	82.4	229–230[a]	
2,3,4,5-tetrachloro	98.1		
2,3,4,6-tetrachloro	92	266–276	
pentachloro	224.5–225.5	301	

[a]At 95.4 kPa (716 mm Hg).

are available from direct chlorination of monochlorotoluenes. 2,3-Dichlorotoluene is best prepared by the Sandmeyer reaction on 3-amino-2-chlorotoluene. The chlorination of toluene and o- and p-chlorotoluenes produces mixtures of 2,3,6- and 2,4,5-trichlorotoluenes containing small amounts of the 2,3,4,- and 2,4,6- isomers. 2,3,4,6-Tetrachlorotoluene is prepared from the Sandmeyer reaction on 3-amino-2,4,6-trichlorotoluene. Pentachlorotoluene is formed by the ferric chloride catalyzed chlorination of toluene in carbon tetrachloride or hexachlorobutadiene.

Health and Safety

Monochlorotoluenes are slightly toxic.

Uses

Major use is in the manufacture of p-chlorobenzotrifluoride. Isomers are widely used as solvents and herbicide intermediates.

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BENZYL CHLORIDE, BENZAL CHLORIDE, AND BENZOTRICHLORIDE

Benzyl Chloride

Benzyl chloride, ((chloromethyl)benzene, α-chlorotoluene), C_6H_5-CH_2Cl, is a colorless liquid with a pungent odor; fp $-39.2°C$, bp $179.4°C$, d_4^4 1.114 g/cm^3. Thirty-six binary and nine ternary azeotropic systems containing benzyl chloride have been reported. Benzyl chloride is insoluble in cold water, decomposes slowly in hot water to give benzyl alcohol, and is miscible in all proportions with most organic solvents at room temperature.

Manufacture. Benzyl chloride is manufactured by the thermal or photochemical chlorination of toluene at 65–100°C. Various materials, eg, phosphorus pentachloride or sulfuryl chloride, are reported to catalyze side-chain chlorination. These compounds and others such as amides also reduce ring chlorination by complexing metallic impurities. Commercial chlorination is carried out either batchwise or continuously in glass-lined or nickel reactors. To reduce the risk of decomposition during distillation, additives such as lactams and amines are used; lime, sodium carbonate, and triethylamine are used as stabilizers during storage and shipment.

Benzal Chloride

Benzal chloride, ((dichloromethyl)benzene, α,α-dichlorotoluene, benzylidene chloride), $C_6H_5CHCl_2$, is a colorless liquid with a pungent, aromatic odor; fp $-16.4°C$, bp $205.2°C$, d_{11}^{11} 1.256 g/cm^3. Eight binary

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cost is $0.153/h. The lamp produces $(0.398)(0.720)(7.5) = 2.149$ mol/h. Therefore, the lamp depreciation cost per mole is given by

$$\text{lamp depreciation cost per mole} = \frac{\text{cost/h}}{\text{mol/h}} = \frac{0.153}{2.149} = \$0.071$$

The total photochemical cost per mole is expressed as

$$\text{total cost per mole} = \frac{\text{electrical cost}}{\text{mol}} + \frac{\text{depreciation cost}}{\text{mol}}$$

$$= \$0.140 + 0.071$$

$$= \$0.211$$

If the molecular weight of the product is 200, the photochemical cost per kilogram is $1.06. A molecular weight of 100 would lead to a photochemical cost of $2.11/kg. Additional costs for immersion wells, piping, raw materials, purification, etc, must be added to determine the total manufacturing cost.
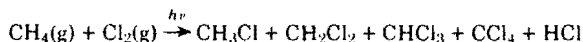
Uses

Free-Radical Reactions. *Chlorinations.* Photochlorinations are important to industry because the lower temperatures at which they occur limit undesirable side reactions. High quantum yields, $\Phi > 100$, are common, so that rates can be high with low capital and electrical requirements. Light of $\lambda = 313$–366 nm, which is the principal uv emission region of the mercury arc, causes chlorine dissociation, and the subsequently formed free radicals can react with hydrocarbons.
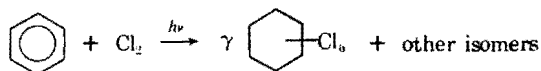
Among the industrially significant chlorinations are production of trichloroethane, a degreasing solvent (17):

$$Cl_2CHCH_3(g) + Cl_2(g) \xrightarrow{h\nu} CH_3CCl_3 + HCl$$
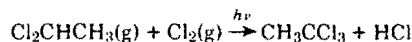
chlorination of methane:

$$CH_4(g) + Cl_2(g) \xrightarrow{h\nu} CH_3Cl + CH_2Cl_2 + CHCl_3 + CCl_4 + HCl$$
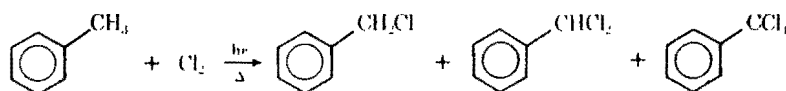
and production of lindane:

(see Chlorocarbons and chlorohydrocarbons).

The active insecticidal ingredient in the benzene hexachloride mixture is the gamma isomer known as gammexane or lindane. The quantum yield is ca 2500 (18), but the chemical yield is only ca 15%. In 1978, U.S. sales exceeded 300 metric tons.

The reaction of chlorine and toluene (qv) is carried out using uncooled lamps; the heat from the lamps and the heat of reaction maintain the refluxing of the toluene. The yield is 90% and the ratio of benzyl chloride to benzal chloride to benzotrichloride